REMARKS

Claims 1-3, 12, 13, 16-19, 26, 31-33, 43-45, 57, 61, 62 and 94-107 are pending in this application. Claims 94 and 101-102 are canceled herein without prejudice. Claims 1-3, 12, 16, 26, 31-33, 43-45, 57, 61, 62, 95-100 and 103-107 are amended herein for clarity to more particularly define the invention. Support for these amendments is found in the language of the original claims and throughout the specification, as set forth below. No new matter is added by these amendments and their entry is respectfully requested. In light of these amendments and the following remarks, applicants respectfully request reconsideration of this application and allowance of the pending claims to issue.

I. Claim objection

The Office Action states that claims 32-33 are objected to as being improperly dependent from claim 31.

Claims 32-33 are amended herein to recite the transgenic tobacco plant of claim 31, rather than a method and are now proper dependent claims. Thus, this objection has been rendered moot and applicants respectfully request its withdrawal.

II. Rejection under 35 U.S.C. § 112, first paragraph (new matter)

The Office Action states that claims 1-3, 12-13, 16-19, 43-45, 57, 61-62 and 94-107 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly introducing new matter. Specifically, the Office Action states that claim 1 and claims 94-107 recite a nucleic acid greater than or equal to 30, 50, 75, 100, 125, 150 and 200 consecutive nucleotides of SEQ ID NO:1, which in the Examiner's view are drawn to new matter.

Claims 1, 95, 96, 97, 98, 99 and 100 as presented herein recite a nucleic acid comprising at least 30, 50, 75, 100, 125, 150 and 200 consecutive nucleotides of SEQ ID NO:1 or its complement, respectively. Support for these claims is found throughout the specification as filed, including for example, on page 6, lines 15-18; page 10, lines 14-28; page 11, lines 4-7,

page 23, lines 4-7; page 24, lines 3-6, page 15, lines 2-5 and n original claims 35, 36, 53, 54, 58 and 59. Further support for fragments of the nucleotide sequence of SEQ ID NO:1 or its complement in embodiments of this invention can be found, for example, on page 3, lines 5-6, 12-13, 18 and 27-30; page 4, lines 3-5; page 6, lines 5-6 and 12; page 8, lines 10-16; page 8, line 21 through page 9, line 1; page 9, lines 2-7; page 11, lines 8-15; and page 12, lines 17-22. Thus, the claims as presented herein do not contain any new matter and applicants respectfully request withdrawal of this rejection.

III. Rejection under 35 U.S.C. § 112, first paragraph (written description)

The Office Action states that claims 1-3, 12-13, 16-19, 26, 31-33, 43-45, 57, 61 and 62 remain and new claims 94-107 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. The Office Action states that the claims are directed to SEQ ID NO:1 and fragments of SEQ ID NO:1 and that because applicants have not described a structure shared in common between the claimed fragments and that is correlated with the claimed antisense activity, the written description requirement has not been satisfied.

Applicants respectfully traverse this rejection on the basis that the claims as presented herein are adequately supported in the specification. Specifically, the claims of the present invention are directed to various sized of fragments of the nucleotide sequence of SEQ ID NO:1 or its complement. Representative examples of a large number of such fragments are provided throughout the specification as set forth above in response to the new matter rejection. All of the fragments of this invention share the common structural feature of comprising at least part of the nucleotide sequence defined in the specification as SEQ ID NO:1 and the common functional feature of hybridizing to quinolate phosphoribosyl transferase messenger RNA. Thus, it would be apparent to one of ordinary skill in the art that applicants were indeed in possession of all members of the genus of fragments of the nucleotide sequence of SEQ ID NO:1 that are encompassed by the claims.

Furthermore, applicants respectfully point out that adequate written support does not require that the application contain an exhaustive enumeration of all possible fragments of the nucleotide sequence of SEQ ID NO:1. Such information is readily obtainable from the nucleotide sequence of SEQ ID NO:1 as provided in the specification and, as noted above, numerous examples of fragments of specific sizes are provided throughout the specification. The USPTO itself has cautioned that "[t]he absence of definitions or details for well-established terms or procedures should not be the basis of a rejection under 35 U.S.C. § 112, para. 1, for lack of adequate written description" (Revised Interim Written Description Training Examples, "Synopsis of Application of Written Description Guidelines").

Furthermore, with regard to establishing a representative number of species of the genus of fragments of the nucleotide sequence of SEQ ID NO:1 that hybridize to QPRTase mRNA, the Written Description Guidelines [*Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶1, "Written Description" Requirement,* Federal Register 66, p. 1105 col. 3 (Jan. 5, 2001)] indicate that where there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the species. In the present invention, there is not substantial variation between members of the claimed genus, as all members of the genus have in common a portion of the nucleotide sequence of SEQ ID NO:1 as a structural feature, which sequence is provided in the specification as filed.

The applicants also point out that the Written Description Guidelines state that "[d]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." In the present invention, the claimed genus is readily identified by the limitations set forth in the specification as being defined by the sequence of SEQ ID NO:1 and it is apparent that individual support for each species of the genus is not required for one of ordinary skill in the art to readily identify any of the nucleic acids claimed in this invention.

The Written Description Guidelines also state that the written description requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice. Applicants respectfully point out that the present application describes the reduction to practice of hybridization of fragments of the nucleotide sequence of SEQ ID NO:1 to QPRTase mRNA in Examples 2, 3 and 4 on pages 22-25 of the specification as filed.

Applicants also note that in the Revised Interim Written Description Guidelines Training Materials, the Decision Tree presented on page 9, for evaluating whether a genus in an original claim meets the written description requirement, shows that a determination of what is a representative number of species "...depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed or claimed." In the present invention, one of skill in the art would readily recognize that applicants were in possession of the nucleotide sequence of SEQ ID NO:1 and therefore the possession of any fragments thereof as recited in the claims and as defined in the specification to have the functional requirement of hybridizing to QPRTase mRNA. These structural and functional characteristics, coupled with the disclosed correlation between structure and function (i.e., a nucleic acid fragment of the sequence of SEQ ID NO:1 that hybridizes with QPRTase mRNA) define the necessary common attributes or features of the elements possessed by all members of the genus of the claimed invention. Therefore, the specification provides a description of all of the elements that are essential to the operation and function of the genus as presented in the claimed invention and that are needed in order to meet the written description requirement.

Thus, the claimed invention as a whole is readily identifiable, and any member of the claimed genus would be readily recognized by one of skill in the art. Accordingly, the skilled artisan would conclude that applicants were indeed in possession of the claimed invention as a whole. Therefore, the claimed invention meets the written description requirements of 35 U.S.C. § 112, first paragraph, and applicants respectfully request that this rejection be withdrawn.

IV. Rejection under 35 U.S.C. § 112, first paragraph (enablement)

The Office Action states that claims 1-3, 12-13, 16-19, 26, 31-33, 43-45, 57, 61 and 62 remain and new claims 94-107 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

Applicants respectfully traverse this rejection. Specifically, it is well established that the test of enablement under 35 USC §112, first paragraph, is not whether any experimentation is necessary but rather is whether one skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. *See, e.g.,* MPEP 2164.01. Further, it is well settled that "a patent need not teach, and preferably omits, what is well known in the art." *Id.* In addition, in order to make a rejection, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *See* MPEP 2164.04. It is also specifically noted that a specification that contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the claimed subject matter must be taken as in compliance with the enablement requirement unless there is a reason to doubt the objective truth of the statements contained therein.

In determining whether or not the enablement requirement is satisfied in any particular case and whether any necessary experimentation is undue, reference is typically made to the factual inquiries specified in *In re Wands*, as described in MPEP § 2164.01(a). The inquiries include the following:

(A) The breadth of the claims;

(B) The existence of working examples;

(C) The nature of the invention;

(D) The state of the prior art;

(E) The level of one of ordinary skill;

(F) The level of predictability in the art;

(G) The amount of direction provided by the inventor; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

When the above factors are evaluated in the context of the present invention, it is respectfully submitted that the enablement requirement is clearly satisfied. Hence, each of these factors is discussed in this context in greater detail below.

(A) The breadth of the claims.

The invention as claimed herein is directed to an isolated nucleic acid that hybridizes to a tobacco quinolate phosphoribosyl transferase messenger RNA, wherein said nucleic acid comprises at least 30 consecutive nucleotides of SEQ ID NO:1 or its complement. The claims also recite various embodiments wherein the nucleic acid comprises at least 50, 75, 100, 125, 150 or 200 consecutive nucleotides of SEQ ID NO:1 or its complement, as well as methods employing the nucleic acids of this invention to produce transgenic plants having reduced QPRTase expression and reduced nicotine and the plants so produced. Support for the claims as presented herein is found throughout the specification, as set forth in detail above in response to the new matter rejection. Thus, no new matter is included within the claims as presented herein.

The claims as presented herein are well focused and their breadth is clearly defined to encompass a specific genus of nucleic acids having common structural and functional characteristics as described above. One of ordinary skill in the art could readily obtain any nucleic acid encompassed within the claimed genus according to well known protocols and test any such nucleic acid for the ability to hybridize with QPRTase mRNA according to protocols as set forth in the Examples section of the instant specification and as were well known in the art at the time of this invention. Thus, it is respectfully submitted that the claims are well focused and their breadth is clearly defined within the disclosure of the specification. Therefore, it is submitted that this factor weighs in favor of the applicants.

(B) The existence of working examples.

It is well settled that the presence of working examples is not required to satisfy the enablement requirement. *In re Strahilevtz*, 212 USPQ 561, 563 (CCPA 1982); MPEP 2164.02. Furthermore, the courts have noted that the specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue experimentation. *See, e.g., In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

As noted above, several working examples of the claimed invention are described in Examples 2, 3 and 4 of the specification. Applicants also respectfully submit that the present invention is disclosed in such a manner that one skilled in the art is able to practice it without undue experimentation, even in the absence of the working examples provided. This assertion is supported by the numerous publications cited in the specification on pages 9-10 and 16-17 and by the long list of publications provided herewith as Appendix A, describing the successful use of antisense technology in plants and in other organisms both at the time of the present invention and subsequently. Such publications demonstrate that the state of the art of antisense technology was well developed at the time of filing of the present application, particularly with regard to the use of antisense fragments that hybridize with a target mRNA.

In the present invention, as the Examiner acknowledges, the instant specification is clearly enabled for the use of the entire sequence of SEQ ID NO:1 as an antisense molecule to reduce QPRTase expression and nicotine production in tobacco cells. Therefore, armed with such teachings of the successful application of the methods of this invention and the knowledge of the sequence of SEQ ID NO:1, one of ordinary skill in the art could readily produce and test any fragment of the full sequence for antisense activity without undue experimentation, based on the teachings of the specification as well as the guidance in the art that antisense fragments of many sizes were known to be functional in a variety of cells to inhibit expression of a variety of genes. Thus, this factor also weighs in favor of the applicants.

(C). The nature of the invention, (D) the state of the prior art and (E) the relative skill of those in the art.

Applicants respectfully submit that these three factors also weigh in their favor. In particular, the nature of the invention becomes the backdrop to determine the state of the art and the level of skill possessed by one skilled in the art (M.P.E.P. § 2164.05(a)). Applicants' invention pertains to nucleic acid fragments of SEQ ID NO:1 that hybridize to QPRTase mRNA. The techniques utilized for making and testing the nucleic acids of the present invention are standard nucleic acid manipulations that were well known and routine in the art at the time the application was filed.

Furthermore, the level of skill in this field is high, and those in the field have ready access to the prior art, which describes the well-established techniques needed to make and use the present invention as claimed and provides numerous examples of the successful application of these techniques in various settings. Not only were the scientific publications described above available to one of skill in the art at the time of this invention for guidance in carrying out the methods employed in the present invention without undue experimentation, the patent literature available at the time of this invention also contained numerous examples of nucleic acid fragments and their use in various plant systems (see, e.g., US Patent Nos. 4,801,540, 5,107,065, 5,453,566, 5,569,831).

Thus, applicants respectfully submit that these three factors- the nature of the invention, the state of the prior art and the relative skill of those in the art, each weigh in their favor.

(F) The level of predictability in the art, (G) the amount of direction provided by the inventor and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Applicants respectfully submit that these three factors also weigh in their favor. In particular, although the biological sciences are generally categorized as "unpredictable," the courts have long and repeatedly emphasized that the issue is not predictability *per se*, but the

type of work and experimentation acceptable in the particular field, or fields, of the invention. For example, in *In re Angstadt,* the Court of Customs and Patent Appeals cautioned that:

> If [our prior decision stands] for the proposition that the disclosure must provide "guidance which will enable one skilled in the art to determine, *with reasonable certainty before performing the reaction,* whether the claimed product will be obtained,... then *all* "experimentation" is "undue," since the term "experimentation" implies that the success of the particular activity is *uncertain.* Such a proposition is contrary to the basic policy of the patent act...."

In re Angstadt, 537 F. 2d 498, 503, 190 USPQ 214, 218-219 (CCPA 1976). The court went on to emphasize that "the key word is 'undue', not 'experimentation'." *Id* at 504, 190 USPQ at 219.

The court has further stated that "...a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988) (quoting *In re Jackson*, 217 USPQ 804, 807 (CCPA 1982)). In *Wands*, claims to antibodies that required a screening procedure to isolate the desired hybridoma cells from an enormous number of other cells present in the reaction mixture were held to not require experimentation that was "undue." *Id.*, 8 USPQ 2d at 1406. The amount of effort required to make the antibodies was "not excessive." *Id.*, 8 USPQ 2d at 1407. Similarly, applicants submit that the experimentation needed in the case of the presently claimed invention is not only routine in the art but that the instant specification provides more than sufficient guidance with respect to the direction in which the experimentation should proceed and what results to expect.

As discussed above, the presently claimed invention uses the well-known techniques of obtaining and then testing various nucleic acid fragments of a defined nucleotide sequence for antisense activity. As would be clear to the ordinary artisan upon reading the publications described herein, fragments of a complete cDNA sequence have been used routinely from the early days of antisense and sense suppression of endogenous genes in plants, continuing up to the

present. Thus, given the complete cDNA or coding sequence of a target protein, it would be trivial and certainly not "undue" for the ordinary artisan to produce any number of constructs with a shorter sequence and identify which constructs have the desired activity.

Moreover, applicants respectfully point out that the Court of Appeals for the Federal Circuit has held that it is not necessary for the specification or claims to list all operative embodiments, or to exclude all inoperative embodiments, stating: "Even if some of the claimed combinations [are] inoperative, the claims are not necessarily invalid. 'It is not a function of the claims to specifically exclude ... possible inoperative substances...'." *Atlas Powder Co. v. DuPont*, 750 F.2d 1569; 224 USPQ 409 (CAFC 1984). All that is required by § 112 is that one skilled in the art may determine the inoperative embodiments with no more than routine skill. For all of the reasons set forth herein, the applicants submit that this standard is satisfied in the present application.

Furthermore, the attached list of references also demonstrates that it was well known in the art that RNA-mediated suppression of gene expression occurs via mechanisms that include the generation of short oligonucleotides (ca. 21-23 nucleotides) that are generated by cleavage of larger molecules and that these small RNAs can direct destruction of RNAs that contain nearly exact complements. Such teachings would further lead one of skill in the art to produce and test short fragments of a full length sequence for antisense activity.

In summary, in a determination of whether the enablement requirement is satisfied, the Examiner must consider all the evidence related to each of above eight factors and any conclusion of non-enablement must be based on the evidence as a whole. *In re Wands*, 858 F.2d, 731, at 737, 740, 8 USPQ 2d 1400, at 1404, 1407 (Fed. Cir. 1988). When the evidence as a whole is considered, applicants respectfully submit that the claimed invention does not require undue experimentation, and thus the invention as claimed herein satisfies the requirement for enablement. Applicants therefore respectfully request that this rejection be withdrawn.

V. Rejection under 35 U.S.C. §101

The Office Action states that claims 26 and 43-45 are rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter on the basis that the claimed inventions encompass untransformed plants and seeds, which are a product of nature and thus, unpatentable.

Claims 26 and 44 as presented herein recite a tobacco seed that comprises the nucleic acid of claim 1. Furthermore, clams 43 and 45 as presented herein recite a progeny of a plant, wherein the progeny is a transgenic plant. Thus, the plants and seeds of these claims are transgenic plants and seeds, which are not a product of nature, and are therefore patentable. This rejection has therefore been overcome and applicants respectfully request its withdrawal.

VI. Double patenting rejection

The Office Action states that claims 1-3, 12-13, 16-19, 26, 31, 43-45 and 57 remain and new claims 94-107 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-32 of U.S. Patent No. 6,586,661. The Office Action states that although the conflicting claims are not identical, they are not patentably distinct from each other because they are both directed to an isolated DNA comprising the DNA sequence of SEQ ID NO:1, which encodes a quinolate phosphoribosyl transferase, a DNA construct thereof, transgenic plants and seeds transformed therewith, and methods of use.

Included herewith is a Terminal Disclaimer that disclaims any patent term for claims issued in the present application that would extend beyond the patent term of U.S. Patent No. 6,586,661. Thus, this rejection has been overcome and applicants respectfully request its withdrawal.

Having addressed all of the issues raised by the Examiner in the present Office Action, applicants believe the present application to be in condition for allowance, which action is respectfully requested. The Examiner is invited and encouraged to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue.

The Commissioner is authorized to charge Deposit Account No. 50-0220 in the amount of $3080.00 ($2160.00 as fee for a five month extension of time after filing a Notice of Appeal, $130.00 as fee for a Terminal Disclaimer and $790.00 as fee for a Request for Continued Examination). This amount is believed to be correct. However, the Commissioner is authorized to charge any deficiency related to this filing or credit any overpayment to Deposit Account No 50-0220.

Respectfully submitted,

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CERTIFICATION OF TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with 37 CFR § 1.6(a)(4) to the U.S. Patent and Trademark Office on August 20, 2007.

Tracy Wallace